CLAIMS

1/. Nucleotide sequence, characterized in that it is constituted by or in that it comprises at least one of the nucleic acid sequences corresponding to the genes called ureE, ureF, ureG, ureH and urel represented by the nucleotide sequences shown in Figure 4 or any part of at least one of these nucleic acid sequences.

2/. Nucleotide sequence according to Claim 1, characterized in that it is modified by deletion, addition, substitution or inversion of one or more nucleotides so that the functional properties of the polypeptides encoded in these modified sequences are either conserved or attenuated, even deleted, as compared with the properties of the polypeptides UreE, UreF, UreG, UreH or UreI as expressed by H. pylori or so that this modified sequence does not express a polypeptide in H. pylori.

3/. Nucleotide sequence according to Claim 1 or Claim 2, characterized in that it is constituted by or in that it comprises :

a) the set of the nucleic acid sequences corresponding to the genes called ureE, ureF, ureG, ureH and urel and represented by the nucleotide sequences shown in Figure 4 or,

b) the set formed by the (variant) nucleic acid sequences corresponding to these genes modified independently of each other such that the set of these variants codes for polypeptides having a functional homology with the polypeptides UreE, UreF, UreG, UReH or UreI such as expressed by H. pylori or conversely codes for modified polypeptides which attenuate or even abolish the functional properties of the polypeptides UreE, UreF, UreG, UreH or UreI such as expressed by H. pylori or is no longer expressed as polypeptides.

4/. Nucleotide sequence characterized in that it is a fragment of a nucleotide sequence according to either of the Claims 1 or 2, the said fragment comprising at least 15 nucleotides, it being possible to select this fragment from :

- fragments which have conserved the capacity to code for polypeptides having a functional homology with the polypeptides as obtained by expression of a gene selected from ureE, ureF, ureG, ureH and urel in H. pylori ;
- fragments coding for any part of the polypeptides

(SEQ. ID NOS: 4, 7 and 3 respectively)

a UreE, UreF, UreG, UreH and UreI such as are produced in H. pylori, and in particular coding for peptides or parts of polypeptides recognized by antibodies directed against H. pylori or capable of behaving as haptens or immunogens;

- fragments lacking the capacity to code for the polypeptides of H. pylori such as expressed by the genes ureE, ureF, ureG, ureH and ureI (SEQ. ID NO: 1)

a

- fragments coding for polypeptides or peptides having properties which have been attenuated or abolished as compared with the properties of polypeptides encoded in the genes ureE, ureF, ureG, ureH and ureI of H. pylori (SEQ. ID NO: 1)

a

5/. Nucleotide sequence according to any one of the Claims 1 to 4, characterized in that it is associated with nucleic acid sequences corresponding to the structural genes ureA and ureB which code for the urease subunits in H. pylori.

6/. Nucleotide sequence according to any one of the Claims 1 to 5, characterized in that it is associated with the genes ureA, ureB, ureC and/or ureD which code for the urease in H. pylori.

7/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureE sequence represented by the nucleotides 800 to 1309 of the sequence shown in Figure 4 (SEQ. ID NO: 1) or to any part of this sequence provided that it hybridizes under stringent conditions with the ureE sequence or with the sequence complementary to this sequence.

a

8/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureF sequence represented by the nucleotides 1324 to 2091 of the sequence shown in Figure 4 (SEQ. ID NO: 1) or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureF sequence or with the sequence complementary to this sequence

a

9/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureG sequence represented by the nucleotides 2123 to 2719 of the sequence shown in Figure 4 (SEQ. ID NO: 1) or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureG sequence or with the sequence complementary to this sequence

a

10/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureH sequence

represented by the nucleotides 2722 to 3516 of the sequence shown in Figure 4 (SEQ ID NO:1) or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureH sequence or with the sequence complementary to this sequence.

11/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureI sequence represented by the nucleotides 211 to 795 of the sequence shown in Figure 4 (SEQ. ID NO: 1) or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureI sequence or with the sequence complementary to this sequence.

12/. Nucleotide sequence according to Claim 7, characterized in that it corresponds to the following nucleotide sequence or in that it comprises this sequence (SEQ. ID NO:8):

GCG AAA ATA TGC TAT GAA ATA GGA AAC CGC CAT

13/. Nucleotide sequence characterized in that it is constituted by a nucleotide sequence according to any one of the Claims 1 to 12, the said sequence being labelled.

14/. Nucleotide primer characterized in that it comprises a nucleotide fragment such as that derived from a sequence according to any one of the Claims 1 to 12 comprising about 18 to about 30, and preferably about 25 to about 30 nucleotides for use in a gene amplification reaction.

15/. Nucleotide sequence characterized in that it hybridizes under stringent conditions with a sequence according to any one of the Claims 1 to 14.

16/. Use of a primer according to Claim 14 for the in vitro detection of an infection due to H. pylori in a biological sample subsequent to gene amplification reactions.

17/. Use of a probe according to Claim 13 for the in vitro detection in a biological sample of an infection due to H. pylori, optionally subsequent to gene amplification reactions.

18/. Polypeptide characterized in that it corresponds to one of the polypeptides UreE, UreF, UreG, UreH or UreI shown in Figure 4 (SEQ. ID NOs: 4-7 and 3, respectively) or any part of at least one of these polypeptides for example a polypeptide represented by the sequence:

Ala Lys Ile Cys Tyr Glu Ile Gly Asn Arg His.

19/. Polypeptide according to Claim 18 in a form modified by addition, substitution, deletion or inversion of one or more amino

acids in order to attenuate or even abolish its properties in the regulation ~~and/~~or maturation of the urease ~~such as that~~ expressed by the polypeptides UreE, UreF, UreG, UreH or UreI in H. pylori (SEQ. ID NOS: 4-7 and 3, respectively).

20/. Recombinant vector, characterized in that it contains a sequence according to any one of the Claims 1 to 12.

21/. Recombinant vector according to Claim 20, characterized in that it is a cosmid or a plasmid.

22/. Recombinant vector according to either of the Claims 20 or 21, characterized in that it is the plasmid pILL753 contained in E. coli HB101, deposited with the CNCM on 3 October 1991 under the number I-1148.

23/. Recombinant vector according to either of the Claims 20 or 21, characterized in that it is the plasmid pILL763 contained in E. coli HB101 deposited with the CNCM on 3 October 1991 under the number I-1149.

24/. Recombinant strain of H. pylori characterized in that it exhibits a mutation in at least one of the genes ureE, ureF, ureG, ureH, ureI, or ureA or ureB under conditions such that the recombinant strain expresses a urease-negative phenotype, or exhibits attenuation of the effects of urease, in particular its pathological effects.

25/. Recombinant strain of H. pylori according to Claim 24, characterized in that it has a mutation in the ureG gene (SEQ. ID NO: 1).

26/. Recombinant strain of H. pylori according to Claim 24, characterized in that it has a mutation in the ureA gene.

27/. Recombinant strain of H. pylori according to Claim 24, characterized in that it has a mutation in the ureB gene.

28/. Recombinant strain of H. pylori according to any one of the Claims 24 to 27, characterized in that it is the mutant strain N6 (NCIMB No. 40512).

29/. Recombinant cell host different from H. pylori, characterized in that it is transformed by a sequence according to any one of the Claims 1 to 12 or 15 under conditions making possible its expression in the host.

30/. Recombinant cell host according to Claim 29, characterized in that it is a strain of H. pylori which comprises a nucleotide sequence according to any one of the Claims 2 to 12 or 15.

31/. Recombinant cell host according to Claim 30, such as that produced by mutation of the N6 strain of H. pylori, deposited with the NCIMB on 26 June 1992 under the NCIMB number 40512 in at least one of the genes ureE, ureF, ureG, ureH and ureI, (SEQ. ID NO: 1)

32/. Recombinant cell host according to any one of the Claims 29 to 31, characterized in that it is an E. coli strain modified by a nucleotide sequence according to any one of the Claims 1 to 12.

33/. Recombinant cell host according to any one of the Claims 29 to 31, characterized in that its urease activity is attenuated.

34/. Immunogenic composition, characterized in that it contains a recombinant cell host according to any one of the Claims 24 to 33.

35/. Kit for the in vitro diagnosis of an infection due to H. pylori in a defined biological sample, characterized in that it contains :

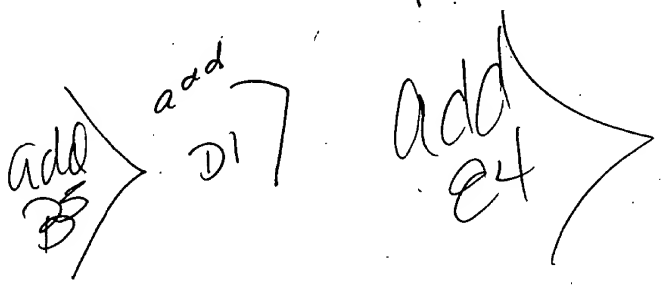
- at least one pair of nucleotide primers according to Claim 13, capable of hybridizing with the 5' and 3' ends of a nucleotide fragment specific for at least one gene selected from ureE, ureF, ureG, ureH and ureI, (SEQ. ID NO: 1)
- reagents necessary for the extraction of the nucleic acids from the treated sample,
- reagents for carrying out the polymerization of the said nucleotide fragment, from nucleotide primers, in particular polymerization enzymes in sufficient quantity to achieve the amplification of the fragment which it is desired to amplify,
- at least one nucleotide sequence which can be used as probe and is capable of hybridizing under defined conditions with the amplified nucleotide fragment,
- optionally, agents for revealing the hybridization.

36/. Kit for the in vitro diagnosis of an infection due to H. pylori, characterized in that it contains :

- a defined quantity of probe according to Claim 13,
- a medium suitable for carrying out a hybridization reaction between the nucleic acid of H. pylori to be detected and the probe,
- reagents for the detection of hybrids possibly formed.

37/. Monoclonal or polyclonal antibody, characterized in that it specifically binds essentially purified and isolated a polypeptide according to either of the Claims 18 or 19 or a fragment of this polypeptide.

38/. Composition for the treatment of an infection due to H.pylori, characterized in that it ~~contains an antibody~~ according to ~~either of the~~ Claims 18 or 19.



CLAIMS

1/. Nucleotide sequence, characterized in that it is constituted by or in that it comprises at least one of the nucleic acid sequences corresponding to the genes called ureE, ureF, ureG, ureH and ureI represented by the nucleotide sequences shown in Figure 4 or any part of at least one of these nucleic acid sequences, with the exception of the portion of the nucleic acid sequence of the ureI gene corresponding to the nucleotides 209-282 of the nucleotide sequences shown in Figure 4 or any fragment of this portion of the ureI gene, the said part being such that the functional properties of the polypeptide which it encodes are either conserved, or attenuated, or even abolished as compared with the properties of the polypeptides UreE, UreF, UreG, UreH or UreI as expressed by H. pylori, or such that this modified sequence does not express a polypeptide in H. pylori..

2/. Nucleotide sequence according to Claim 1, characterized in that it is modified by deletion, addition, substitution or inversion of one or more nucleotides so that the functional properties of the polypeptides encoded in these modified sequences are either conserved or attenuated, even deleted, as compared with the properties of the polypeptides UreE, UreF, UreG, UreH or UreI as expressed by H. pylori or so that this modified sequence does not express a polypeptide in H. pylori.

3/. Nucleotide sequence according to Claim 1 or Claim 2, characterized in that it is constituted by or in that it comprises :

a) the set of the nucleic acid sequences corresponding to the genes called ureE, ureF, ureG, ureH and ureI represented by the nucleotide sequences shown in Figure 4 or,

b) the set formed by the (variant) nucleic acid sequences corresponding to these genes modified independently of each other such that the set of these variants codes for polypeptides having a functional homology with the polypeptides UreE, UreF, UreG, UReH or UreI such as expressed by H. pylori or conversely codes for modified polypeptides which attenuate or even abolish the functional properties of the polypeptides

UreE, UreF, UreG, UreH or UreI such as expressed by H. pylori or is no longer expressed as polypeptides.

4/. Nucleotide sequence characterized in that it is a fragment of a nucleotide sequence according to either of the Claims 1 or 2, the said fragment comprising at least 15 nucleotides, it being possible to select this fragment from :

- fragments which have conserved the capacity to code for polypeptides having a functional homology with the polypeptides as obtained by expression of a gene selected from ureE, ureF, ureG, ureH and ureI in H. pylori ;
- fragments coding for any part of the polypeptides UreE, UreF, UreG, UreH and UreI such as are produced in H. pylori, and in particular coding for peptides or parts of polypeptides recognized by antibodies directed against H. pylori or capable of behaving as haptens or immunogens;
- fragments lacking the capacity to code for the polypeptides of H. pylori such as expressed by the genes ureE, ureF, ureG, ureH and ureI
- fragments coding for polypeptides or peptides having properties which have been attenuated or abolished as compared with the properties of polypeptides encoded in the genes ureE, ureF, ureG, ureH and ureI of H. pylori.

5/. Nucleotide sequence according to any one of the Claims 1 to 4, characterized in that it is associated with nucleic acid sequences corresponding to the structural genes ureA and ureB which code for the urease subunits in H. pylori.

6/. Nucleotide sequence according to any one of the Claims 1 to 5, characterized in that it is associated with the genes ureA, ureB, ureC and/or ureD which code for the urease in H. pylori.

7/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureE sequence represented by the nucleotides 800 to 1309 of the sequence shown in Figure 4, or to any part of this sequence provided that it hybridizes under stringent conditions with the ureE sequence or with the sequence complementary to this sequence.

8/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureF sequence repreented by the nucleotides 1324 to 2091 of the sequence shown in Figure 4,

or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureF sequence or with the sequence complementary to this sequence

9/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureG sequence represented by the nucleotides 2123 to 2719 of the sequence shown in Figure 4, or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureG sequence or with the sequence complementary to this sequence

10/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureH sequence represented by the nucleotides 2722 to 3516 of the sequence shown in Figure 4, or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureH sequence or with the sequence complementary to this sequence.

11/. Nucleotide sequence according to any one of the Claims 1 to 6, characterized in that it corresponds to the ureI sequence represented by the nucleotides 211 to 795 of the sequence shown in Figure 4, or to any fragment of this sequence provided that it hybridizes under stringent conditions with the ureI sequence or with the sequence complementary to this sequence.

12/. Nucleotide sequence according to Claim 7, characterized in that it corresponds to the following nucleotide sequence or in that it comprises this sequence :

GCG AAA ATA TGC TAT GAA ATA GGA AAC CGC CAT

13/. Nucleotide sequence characterized in that it is constituted by a nucleotide sequence according to any one of the Claims 1 to 12, the said sequence being labelled.

14/. Nucleotide primer characterized in that it comprises a nucleotide fragment such as that derived from a sequence according to any one of the Claims 1 to 12 comprising about 18 to about 30, and preferably about 25 to about 30 nucleotides for use in a gene amplification reaction.

15/. Nucleotide sequence characterized in that it hybridizes under stringent conditions with a sequence according to any one of the Claims 1 to 14.

16/. Use of a primer according to Claim 14 for the in vitro detection of an infection due to H. pylori in a biological sample subsequent to gene amplification reactions.

17/. Use of a probe according to Claim 13 for the in vitro detection in a biological sample of an infection due to H. pylori, optionally subsequent to gene amplification reactions.

18/. Polypeptide characterized in that it corresponds to one of the polypeptides UreE, UreF, UreG, UreH or UreI shown in Figure 4 or to any part of at least one of these polypeptides, with the exception of the portion of the polypeptide UreI encoded in the nucleic acid sequence corresponding to the nucleotides 209-282 of the nucleotide sequences shown in Figure 4 or any fragment of this portion, the said part being such that the properties of the said polypeptide in the regulation and/or maturation of the urease as expressed by the polypeptides UreE, UreF, UreG, UreH and UreI in H. pylori are attenuated, even abolished, the said polypeptide corresponding, for example to a polypeptide represented by the sequence :

Ala Lys Ile Cys Tyr Glu Ile Gly Asn Arg His.

19/. Polypeptide according to Claim 18 in a form modified by addition, substitution, deletion or inversion of one or more amino acids in order to attenuate or even abolish its properties in the regulation and/or maturation of the urease such as that expressed by the polypeptides UreE, UreF, UreG, UreH or UreI in H. pylori.

20/. Recombinant vector, characterized in that it contains a sequence according to any one of the Claims 1 to 12.

21/. Recombinant vector according to Claim 20, characterized in that it is a cosmid or a plasmid.

22/. Recombinant vector according to either of the Claims 20 or 21, characterized in that it is the plasmid pILL753 contained in E. coli HB101, deposited with the CNCM on 3 October 1991 under the number I-1148.

23/. Recombinant vector according to either of the Claims 20 or 21, characterized in that it is the plasmid pILL763 contained in E. coli HB101 deposited with the CNCM on 3 October 1991 under the number I-1149.

24/. Recombinant strain of H. pylori characterized in that it exhibits a mutation in at least one of the genes ureE, ureF, ureG, ureH, ureI shown in Figure 4, or ureA or ureB under conditions

such that the recombinant strain expresses a urease-negative phenotype, or exhibits attenuation of the effects of urease, in particular its pathological effects.

25/. Recombinant strain of H. pylori according to Claim 24, characterized in that it has a mutation in the ureG gene.

26/. Recombinant strain of H. pylori according to Claim 24, characterized in that it has a mutation in the ureA gene.

27/. Recombinant strain of H. pylori according to Claim 24, characterized in that it has a mutation in the ureB gene.

28/. Recombinant strain of H. pylori according to any one of the Claims 24 to 27, characterized in that it is the mutant strain N6 (NCIMB No. 40512).

29/. Recombinant cell host different from H. pylori, characterized in that it is transformed by a sequence according to any one of the Claims 1 to 12 or 15 under conditions making possible its expression in the host.

30/. Recombinant cell host according to Claim 29, characterized in that it is a strain of H. pylori which comprises a nucleotide sequence according to any one of the Claims 2 to 12 or 15.

31/. Recombinant cell host according to Claim 30, such as that produced by mutation of the N6 strain of H. pylori, deposited with the NCIMB on 26 June 1992 under the NCIMB number 40512 in at least one of the genes ureE, ureF, ureG, ureH and ureI.

32/. Recombinant cell host according to any one of the Claims 29 characterized in that it is an E. coli strain modified by a nucleotide sequence according to any one of the Claims 1 to 12.

33/. Recombinant cell host according to any one of the Claims 29 to 31, characterized in that its urease activity is attenuated.

34/. Immunogenic composition, characterized in that it contains a recombinant cell host according to any one of the Claims 24 to 33.

35/. Kit for the in vitro diagnosis of an infection due to H. pylori in a defined biological sample, characterized in that it contains :

- at least one pair of nucleotide primers according to Claim 14, capable of hybridizing with the 5' and 3' ends of a nucleotide fragment specific for at least one gene selected from ureE, ureF, ureG, ureH and ureI,
- reagents necessary for the extraction of the nucleic acids from the treated sample,

- reagents for carrying out the polymerization of the said nucleotide fragment, from nucleotide primers, in particular polymerization enzymes in sufficient quantity to achieve the amplification of the fragment which it is desired to amplify,
- at least one nucleotide sequence which can be used as probe and is capable of hybridizing under defined conditions with the amplified nucleotide fragment,
- optionally, agents for revealing the hybridization.

36/. Kit for the in vitro diagnosis of an infection due to H. pylori, characterized in that it contains :

- a defined quantity of probe according to Claim 13,
- a medium suitable for carrying out a hybridization reaction between the nucleic acid of H. pylori to be detected and the probe,
- reagents for the detection of hybrids possibly formed.

37/. Monoclonal or polyclonal antibody, characterized in that it recognizes a polypeptide according to either of the Claims 18 or 19 or a fragment of this polypeptide.

38/. Composition for the treatment of an infection due to H.pylori, characterized in that it contains an antibody according to either of the Claim 37.